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Original Research

The significance of radiological and laboratory findings in the diagnosis of new COVID-19 disease

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Abstract

Aim: The new coronavirus disease (COVID-19), which first appeared in Wuhan, China in December 2019 and spread rapidly throughout the country, has rapidly becoe a pandemic and a global threat within the first months of 2020. In this study, we aimed to compare the laboratory findings of the patients with negative and positive polymerase chain reaction (PCR) tests results due to COVID-19-like findings in chest computed tomography (CT).

Material and Methods: The study included 49 patients admitted to the emergency department with the suspicion of COVID-19 due to the positive findings on chest CT. Nasopharyngeal swabs were taken from each patient. Whole blood count and biochemical parameters were examined, and as a result of swab investigations, the laboratory values of positive and negative results were compared in order to diagnose COVID-19 cases.

Results: A total of 49 patients were included in the study. The swab specimensobtained from the nasopharynx were evaluated using the reverse transcription PCR (RT-PCR) test. While the RT-PCR positivity was observed in 13 patients (Group 1), the RT-PCR negativity was found in 36 (Group 2). The mean age of all participants was 55.7±17.3 years; in Group 1, however in Group 1, the values of leukocyte, lactate dehydrogenase and ferritin were observed to be higher and lymphocyte count was significantly lower, compared with thosein Group 2.

Dicussion: Previous studies have shown that the diagnosis of new COVIDV-19 disease and its clinical features should be based on a comprehensive understanding of radiographic features and laboratory investigations. Patients with clinical suspicion and those with exposure, fever and a history of positive findings on chest CT should be rapidly diagnosed with molecular technology. The RT-PCR test was developed as a widely used method to detect viral RNA. Although the RT-PCR test is considered the gold standard diagnostic method, this method has some limitations. Clinical findings, history, physical examination and radiological findings were compatible with COVID 19 in our study, the RT-PCR test results were negative in some patients.

The new COVID-19 disease is a very contagious condition leading to devastating consequences. Therefore, the clinical, radiological and laboratory findings should be taken into account as a holistic approach in the diagnosing process of new COVID-19 disease.

Keywords

New Coronavirus; Pandemics; Radiology

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Introduction

Corona viruses are undivided positive RNA viruses of the coronaviridae family. Coronaviruses can infect mainly humans, as well as all other mammals [1]. For the first time, the cases of viral pneumonia were reported following contact with the products in a seafood market in Wuhan, Chinain December 2019. Later, the agent was determined to originate from severe acute respiratory syndrome-CoV-2 (SARS-CoV-2), and the disease caused by the coronavirus was named as the new coronavirus disease 2019 (COVID-19) [2]. It has been observed that the clinical findings of SARS-CoV-2 infection in hospitalized patients in Wuhan started as an asymptomatic disease and mild upper respiratory tract infection, and then developed into a broad spectrum accompanied by respiratory failure that could result in severe viral pneumonias [3]. In addition, COVID-19 has been reported to cause the fatality rate of around 2% due to progressive respiratory failure and massive alveolar damage [4]. According to the latest guideline of 2019-nCoV (6th version trial) published by the Chinese Government, it has been reported that the diagnosis of COVID-19 should be confirmed with the reverse transcription-polymerase chain reaction (RT-PCR) test. In addition, the correlation of respiratory functions or blood samples was proposed as a key indicator for hospitalization.

However, due to the limitations in collecting and handling specimens and kit performance, the total positive rate of RT-PCR for throat swab samples was reported to be approximately 30 to 60% in the first presentation [5]. In the current emergency, the low sensitivity of RT-PCR means that many COVID-19 patients may not be diagnosed and will not receive appropriate timely therapeutic interventions, and given the highly infectious nature of COVID-19, such patients pose risks to infect larger populations. In terms of pulmonary challenges, chest computed tomography (CT) is a relatively easy approach to perform, and thus the diagnosis can be implemented more rapidly. In this context, chest CT may be beneficial for the diagnosis of COVID-19. As reported in a previous study, chest CT demonstrates typical radiographic features in almost all COVID-19 patients, including in ground-glass opacities, multifocal irregular consolidation and/or interstitial changes with peripheral distribution [6]. Such CT findings have also been observed in patients with clinical symptoms, but having RT-PCR (-) results. In a study, it has been noted that the current RT-PCR test has limited sensitivity, and chest CT can elucidate pulmonary abnormalities compatible with COVID-19 in patients with negative RT-PCR test results at an early stage [7]. In our study, we aimed to compare other laboratory and clinical findings of the patients with negative and positive RT-PCR results compatible with COVID-19 obtained on chest CT.

Material and Methods

The study enrolled, a total of 49 suspected COVID-19 patients who were admitted to the emergency department and followed-up in Konya Application and Research Hospital of Baskent University between March 2020 and April 2020 were included in the study. Approvals from Baskent University and Ministry of Health Ethics Committee were obtained. Based on the history and clinical features, patients with suspected COVID-19 disease underwent chest CT without contrast. In light of CT findings, those with symptoms such as bilateral ground-glass appearance, peripheral and dorsal consolidation, paving-stone patterns mainly in the middle and zones, multilobar air bronchograms and vascular enlargement were hospitalized. Data such as age, gender and patients'complaints were also recorded. Meanwhile, the laboratory investigations detected on admission were evaluated. The values of leukocyte-white blood count (WBC), neutrophil, lymphocyte, platelet, neutrophil/lymphocyte ratio (NLR), monocyte, C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) were assessed and recorded. Afterward, nasopharyngeal and throat swabs were taken from each patient for the RT-PCR test. The patients with RT-PCR (+) and (-) results were classified into two groups: Group1 and Group2, and other laboratory findings like age, gender and patients' complaints were also compared.

Laboratory Investigation:

Complete blood count (CBC) measurements were performed using a routine electronic blood count device (Cell-Dyne 3700, Abbott, Abbott Park, IL, USA). For the measurements of CRP, LDH, ferritin, AST and ALT, routine biochemistry kits were used. Nasopharyngeal and throat swab tested positive for SARS-CoV-2 PCR.

Statistical Analysis

Statistical analysis was performed with the IBM SPSS Statistic 22 and Python 3.7 software. To visualize the data and interpret them better, box-plot graphs for each variable according to groups are also given below. These graphs show the minimum, first quartile, median (second quartile), third quartile, maximum and outliers values of variables by group.

The results of the descriptive statistics for considered variables were given as mean±standart deviation (SD) (min and max). To check the normality and variance homogeneity, the Shapiro-Wilk normality and the Levene tests were used, respectively. The independent t and Mann- Whitney-U tests were subsequently conducted to examine the differences between the groups. P-value of < 0.05 was considered statistically significant.

Results

The study was conductedin Konya Application and Research Hospital of Baskent University between March 2020 and April 2020. A total of 49 patients whose chest CT findings were compatible with COVID-19disease and aged 18 years and over were included in the study. Thirty-three cases whose chest CT findings werenot evaluated in favor of COVID-19; and those having incompatible clinical features with COVID-19 intheir history were excluded from the study. Among the patients, 29 were men (59.1%), and 20 were women (40.9%); the RT-PCR (-) and RT-PCR (+) were detected in 36 (73.4%) and 13 (26.6%) patients, respectively. Patients with RT-PCR (+) and RT-PCR (-) were named as Group 1 and Group 2. Among all patients in Group 1, cough was seen as the most common complaint followed by shortness of breath, fever, nausea, vomiting and fatigue. However, the most common complaint in Group 2 was fever, and such challenges as shortness of breath, cough, muscle pain, nausea, vomiting and diarrhea were detected as accompanying complaints. The mean age of all patients was 55.7±17.3 years, while the age rates were determined

Table 1. Demographic Features and Laboratory Findings of Groups

Groups	Variables	Mean±SD	Minimum	Maximum
RT-PCR(-)	Age	54.94±17.27	23.00	82.00
	WBC (x10³/mm³)	6.59±3.351	3.69	14.50
	Neutrophil (x10³/mm³)	4.90±3.222	3.280	12.50
	Lymphocyte (x10³/mm³)	1.94±0.96	0.100	5.20
	Platelet (x10³/mm³)	227.83±65.70	128.00	384.00
	CRP(mg/L)	56.14±61.99	0.100	245.00
	LDH(U/L)	245.44±71.21	155.00	470.00
	Ferritin	79.07±70.17	19.50	396.00
	AST	25.89±9.38	16.00	50.00
	ALT	27.72±13.49	11.00	84.00
	Monocyte	0.62±0.26	0.20	1.310
	N/L	5.05±6.41	0.69	27.00
RT-PCR(+)	Age	57.69±18.186	30.00	80.00
	WBC (x10³/mm³)	9.30±4.06	1.160	17.20
	Neutrophil (x10³/mm³)	6.21±3.85	2.30	14.50
	Lymphocyte (x10³/mm³)	1.19±0.426	0.43	2.20
	Platelet (x10³/mm³)	227.92±67.370	155.00	399.00
	CRP(mg/L)	44.90±41.718	0.50	143.00
	LDH	253.46±122.024	126.00	605.00
	Ferritin	156.56±102.816	44.50	353.00
	AST	53.62±66.249	18.00	267.00
	ALT	41.15±21.717	21.00	96.00
	Monocyte	0.6715±0.631	0.28	2.65
	N/L	4.86±4.149	1.37	15.82

WBC: White Blood Cell, CRP: C-reactive protein, LDH: Lactate Dehydrogenase, N /L: Neutrophil to Lymphocyte Ratio, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase

Table 2. Laboratory findings of patients on admission

Variables	Groups	n	Mean±s.d.	Test Statistic value	p value
Age	RT-PCR(-)	36	54.94±17.27	-0.485[a]	0.630
	RT-PCR(+)	13	57.69±18.186		
WBC (x10³/mm³)	RT-PCR(-)	36	6.59±3.351	-2.525[b]	0.012*
	RT-PCR(+)	13	9.30±4.06		
Neutrophil (x10³/mm³)	RT-PCR(-)	36	4.90±3.222	-1.676[b]	0.094
	RT-PCR(+)	13	6.21±3.85		
Lymphocyte (x10³/mm³)	RT-PCR(-)	36	1.94±0.96	2.700[a]	0.010*
	RT-PCR(+)	13	1.19±0.426		
Platelet (x10³/mm³)	RT-PCR(-)	36	227.83±65.70	-0.004[a]	0.997
	RT-PCR(+)	13	227.92±67.370		
CRP(mg/L)	RT-PCR(-)	36	56.14±61.99	0.604[a]	0.549
	RT-PCR(+)	13	44.90±41.718		
LDH	RT-PCR(-)	36	245.44±71.21	-0.285[a]	0.777
	RT-PCR(+)	13	253.46±122.024		
Ferritin	RT-PCR(-)	36	79.07±70.17	-3.014[b]	0.003*
	Positive	13	156.56±102.816		
AST	RT-PCR(-)	36	25.89±9.38	-2.622[b]	0.009*
	RT-PCR(+)	13	53.62±66.249		
ALT	RT-PCR(-)	36	27.72±13.49	-2.594[a]	0.013*
	RT-PCR(+)	13	41.15±21.717		
Monocyte	RT-PCR(-)	35	0.62±0.26	-1.311[b]	0.190
	RT-PCR(+)	13	0.6715±0.631		
N/L	RT-PCR(-)	35	5.05±6.41	-0.835[b]	0.404
	RT-PCR(+)	13	4.86±4.149		

as 57.69±18.186 and 54.94±17.27 in Group 1 and Group 2 respectively. No difference was detected between the average age rates of both groups (p=0.63).

While the average WBC value of the patients in Group 1 was 9.30±4.06, the value was found to be 6.59±3.35 of Group 2. When comparing the WBC values in both groups, the value was found higher in Group-1, and the difference was considered statistically significant (p=0.012). In terms of the average neutrophil values of both groups, no statistically significant difference was observed between the values of both groups (p=0.094). When the lymphocyte values in both groups were compared, the mean lymphocyte value in Group 1 was seen to be lower, and the difference was accepted as statistically significant (p=0.010). As to the NLR values, there was no significant difference between the results of the two groups (p=0.404). In addition, no significant difference was seen between the platelet values of both groups (p=0.99). When the average monocyte counts were compared, it was seen that there was no difference between both groups (p=0.190). In terms of the CRP values of both groups, there was no significant difference betweenthe CRP values of both groups (p=0.549).The difference between the LDH values of both groups wasinsignificant (p=0.777). When the ferritin values of both groups were compared, the mean ferritin value was higher in Group 1 (p=0.003).There was also a significant difference between the mean ALT and AST values between both groups. Both ALT (p=0.013) and AST values (p=0.009) were detected to be higher in Group 1 (Tables 1, 2) (Figures 1, 2, 3).

Discussion

The new COVID-19 disease has become a rapidly raging health issue across the world. SARS-CoV-2 is the seventh member of the coronaviridae family, infecting humans. SARS-CoV2 causes a serious infection in the lower respiratory tract in a similar manner to SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) [10]. The clinical picture of COVID-19 can include such disorders as fever, cough, fatigue, muscle pain, acute respiratory failure progressing with diarrhea and pneumonia, metabolic acidosis, septic shock, coagulopathy and organ failure such as liver, kidney and heart can be seen with fever, cough, fever and fatigue [4].

Considering different age segments prone to the condition, all segments are generally susceptible to COVID-19, regardless of age or gender, and those between 30 and 79 years of age make up 86.6% of all cases [8]. In our study, however, the mean age was 55.7 years, and there was no difference between the mean age of the patients with RT-PCR (+) and (-) test results.

In various studies conducted so far, common symptoms of the hospitalized COVID-19 patients were emphasized as fever (98.6%), fatigue (69.6%), dry cough and diarrhea. In other studies, less common symptoms of COVID-19 were reported to be muscle pain, confusion, headache, sore throat, runny nose, chest pain, sputum production, nausea and vomiting [4,9]. In our study, the most common complaints among the patients with both RT-PCR (+) and RT-PCR (-) test results were also dry cough, fever and shortness of breath.

In diagnosing COVID19, healthcare professionals face many difficulties because laboratory findings and radiographic

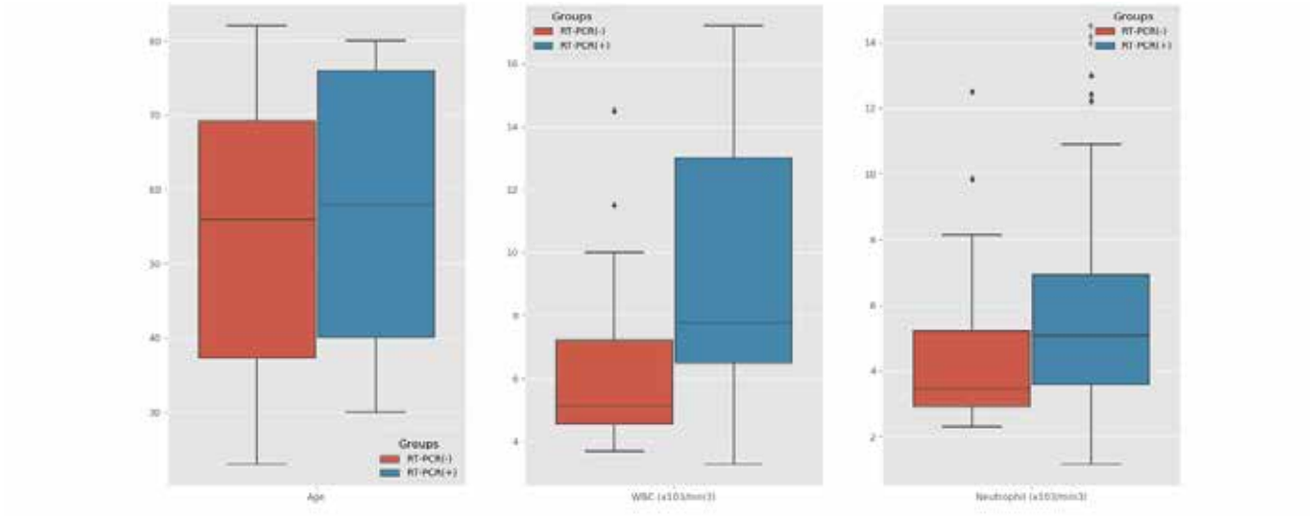

Figure 1. Comparison of Age, WBC and Neutrophil counts in Group 1 and Group 2

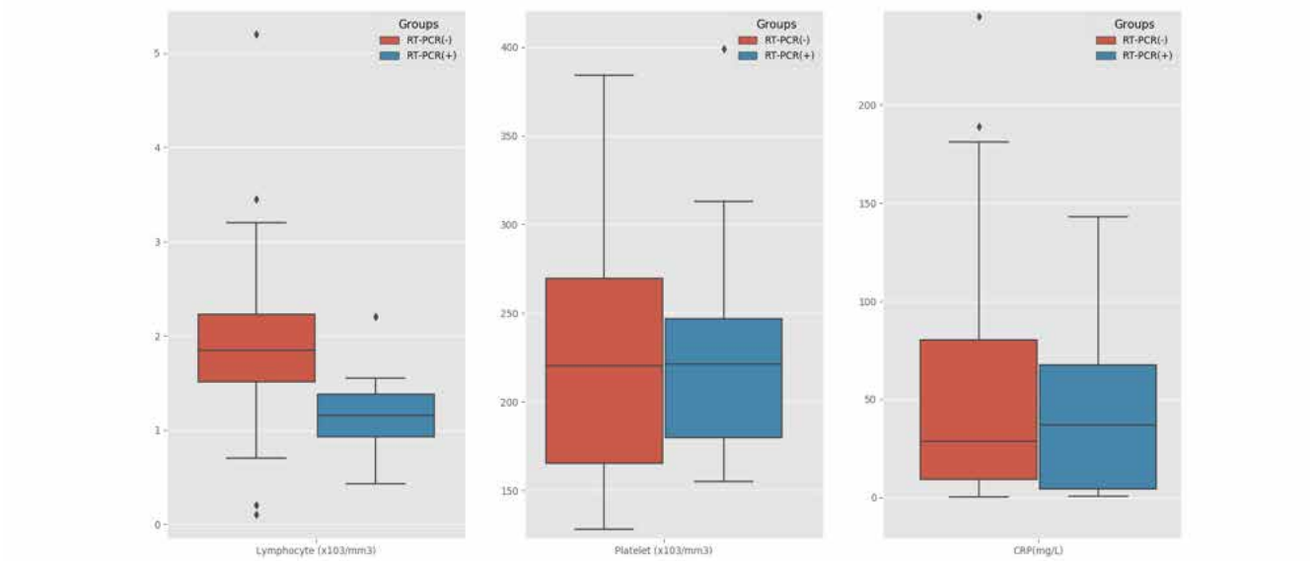

Figure 2. Comparison of Lymphocyte, Platelet and CRP levels in Group 1 and Group 2

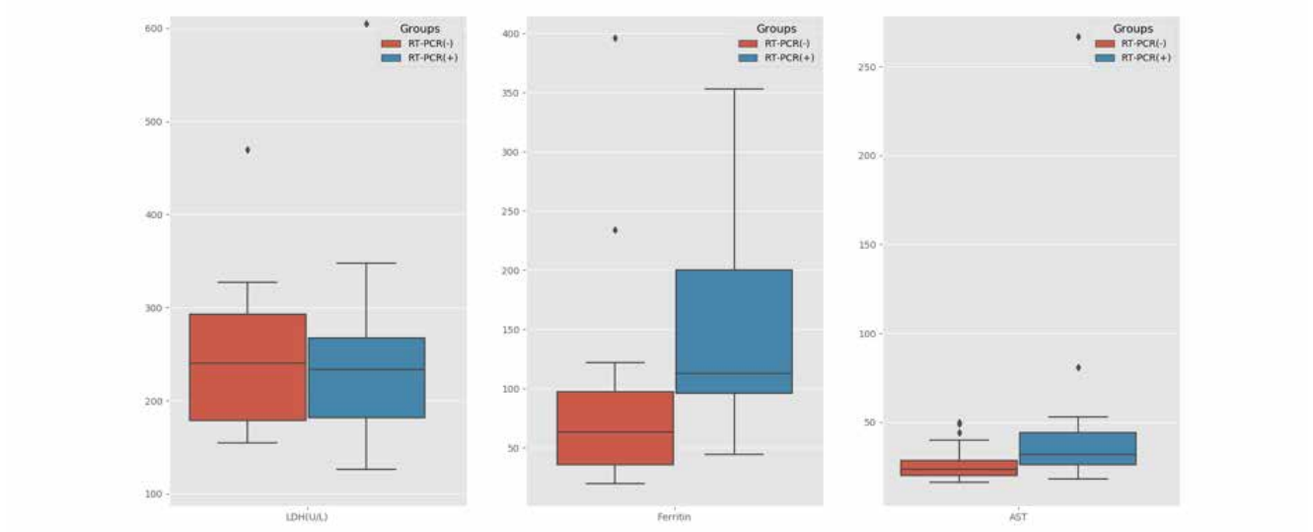

Figure 3. Comparison of LDH, Ferritin and AST levels in Group 1 and Group 2

images may not be always compatible with clinical features and contact history declared by patients [10]. Laboratory tests for COVID-19 include genomic sequencing, RT-PCR and serological methods (enzyme-linked immunosorbent assay (ELISA). In addition, because the appearance of the new coronavirus-induced pneumonia has been varied rapidly, decision-making for early diagnosis and evaluation of the severity of COVID-19, as well as follow-up of patients is highly dependent on the professional experience of specialists. Therefore, there is no definite method for diagnosing this condition yet [11]. Previous studies have shown that the diagnosis of new COVIDV-19 disease and its clinical features should be based on a comprehensive understanding of radiographic features and laboratory tests [12]. In accordance with recommendations in the literature, our study developed an approach, based on the patient's medical history, clinical picture, physical examination, and chest CT and laboratory findings. We constituted a treatment protocol by taking into account that positive or negative RT-PCR test alone was insufficient to detect COVID-19. As a result, clinically suspected patients and those with exposure, fever and a history of positive chest CT findings should be rapidly diagnosed with molecular technology [13].

The RT-PCR test was developed as a widely used method detect viral RNA. Although the RT-PCR test is considered the gold standard diagnostic method, this method has some limitations. These limitations include short-term positivity of nasopharyngeal swabs, false- negative results, cross-contamination of the specimens and inconsistencies in collecting samplesand preparats, which have also reduced the use and reliability ofthe RT-PCR test. Although clinical findings, history, physical examination and radiological findings were compatible with COVID-19 in our study, the RT-PCR test results were detected negative in some patients. There is no clear complete blood or biochemical markers for the diagnosis of COVID-19 yet. In a study, it is reported that the CBC and CRP values increase in severe cases (the guidelines for diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (6^{th} ed.) issued by the National Health Commission of China). Several studies have also found that CBC is significantly higher [14]. Thus, CBC is considered to be the most available, efficient and economic examination. In our study, WBC values in all patients were also higher than normal laboratory values, and the increase was determined to be more pronounced in patients with RT-PCR (+). Lymphocytes play a key role in balancing the immune system and maintaining the inflammatory response in the body. There are studies emphasizing that COVID-19 reduces blood lymphocyte levels during the infection period, and this is important for planning a treatment strategy [15,16].

In another study, the lymphocyte count was found to be significantly lower in patients diagnosed with COVID-19. In this context, it was emphasized that lymphopenia is a valuable marker in the diagnosis process [17]. In our study, however, the mean lymphocyte level was below normal laboratory limitsin all patients, and the level was significantly lower in the patients with RT-PCR (+).

NLR is produced from neutrophils and lymphocytes in circulation and is vital due to its association with inflammation. There are studies emphasizing the course of NLR in COVID-19 cases. However based on the literature, NLR has been shown to be more effective in showing the prognosis of COVID-19. Among the patients with poor prognosis, an increase has been reportedin NLR values [18]. In our study, no difference was detected between the NLR values of the patients with RT-PCR (+) and RT-PCR (-). In some studies, thrombocytopenia was detected in COVID-19 patients. However, in these studies, thrombocytopenia was observed in serious cases, or among those where the disease was severe [17]. In our study, it was seen that the patients' platelet values were within the normal limits, and there was no difference between the patients with RT-PCR (+) and RT-PCR (-). There are also studies demonstrating excessive monocyte and macrophage activation and the related cytokine storm in the development of the complications originated from COVID-19 [19]. Despite this, number of studies investigating the monocyte abnormalities in COVID-19 is patients still limited. A study comparing COVID-19 patients with normal healthy individuals found, no difference between the two groups in terms of monocyte counts, and it was thought that monocytes counts may be proportional to disease severity [20]. In our study, monocyte counts were determined within the normal limits, and no significant change was observed between the monocyte counts in the patients with RT-PCR (+) and RT-PCR (-). Increased CRP is a parameter that can be used for early diagnosis of pneumonia and an important i indicator for the diagnosis and evaluation of severe and infectious pulmonary diseases. CRP levels are associated with the level of inflammation, and the concentration level of CRP is not affected by factors, such as age, gender and physical condition [21].

In a study conducted with patients with COVID-19, increased CRP was stated to be a significant and valuable marker both for diagnosis of pneumonia and for determining its prognosis [22]. The level and course of CRP are recommended for follow-up and treatment of COVID-19 patients. In our study, the CRP values were observed to exceed normal laboratory limits in patients with both RT-PCR (+) and RT-PCR (-) test results.

Previous studies have suggested that LDH plays an important role in detecting lung damage caused by COVID-19 and in determining the severity of the disease [23]. In addition, in another study, the LDH level was considered useful in the diagnosis of COVID 19 [24]. In our study, the LDH level was found to be high in both groups with positive or negative RT-PCR. Moreover, the increase was found to be higher and significant in RT-PCR (+) group, compared to RT-PCR (-) group. In a study conducted with the patients followed due to COVID-19, serum ferritin levels were found to be high in case of severe disease [25]. In our study, the ferritin level was found significantly higher in patients with RT-PCR (+). A study found that patients with RT-PCR (+) had higher AST and ALT values, compared to those with RT-PCR (-) [26]. In our study, AST and ALT values were higher in the RT-PCR (+) group.

Limitation:

In our study, the number of participants was relatively small. In addition, the cases could not be followed-up for a long time, and our study was designed based on laboratory parameters.

Conclusion:

The present study, concluded that radiological and laboratory

findings should be evaluated together, rather than the definitive positivity of the RT-PCR tests in the diagnosis of new COVID-19 disease. We consider that the negativity ofthe RT-PCR test alone is insufficient to rule out the diagnosis of COVID-19, and that a combination of clinical parameters, history, and radiological and laboratory findings will be more meaningful and provide a more accurate diagnosis. In addition, we found that lymphopenia was more prominent during the period when the RT-PCR test results were (+), while neutrophil, AST, ALT, ferritin and LDH levels were higher during the period when the RT-PCR test results were (-). We also consider that further studies including larger series should be beneficial to elucidate the entity.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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